

Replacement Checklist

When looking for non-animal technologies, or alternative approaches to the use of animals in research, there are steps to take in order to thoroughly explore existing opportunities and new approaches to answering a research question.

Similarly, for those reviewing proposals, whether an application for funding or for a licence to use animals in research, there are questions that do not require subject-specialist knowledge that can be asked to provide reassurance that the potential to replace animals has been fully explored.

This checklist aims to:

- Support researchers to identify and assess whether scientifically satisfactory replacement approaches exist in line with current legislation.
- Encourage researchers to plan their research projects from a starting point of avoiding animal use.
- Support members of funding review panels, and Animal Welfare and Ethical Review Bodies (AWERBs) to scrutinise applications and applicants on alternative approaches and how these have been explored.
- Assist AWERBs and institutions to disseminate information on how to more thoroughly explore alternatives at an earlier stage to avoid and replace animal use.
- Help those making decisions about funding animal research to ensure they are supporting research activity that demonstrates full compliance with the 3Rs including the use of alternative methodologies and the avoidance of animal use wherever possible.
- Support editors and reviewers of manuscripts to evaluate compliance of submissions with 3Rs policy of scientific journals.

In the simplest terms, asking the **What, Where, When, Who, How** and **Why** questions should provide information to guide both researchers and reviewers of proposals and applications to ensure a thorough exploration of opportunities to avoid animal use has been performed.

What subject area(s) did the search(es) cover?

Are the search terms and variants used provided?

Searching for potential animal replacements within any given field requires a combination of search terms: subject-specific terms, and keywords focusing on techniques avoiding animal use. Many non-animal approaches with the potential to provide useful data and replace animal use will not necessarily be tagged in literature with '3Rs', 'replacement', or 'alternative' so it is helpful to use terms implying non-animal methods e.g. in vitro, microphysiological, model, assay etc.

Are the search terms relevant to the field of study?

What subject-specific terms were used to try and identify alternative approaches appropriate to the field? Were any variants of keywords included? (Please note that some databases automatically generate variants of search terms)

Is there anything missing from search methodology?

Where was information obtained?

Which databases were searched?

Has a list of the databases or other sources of information been provided? Were multiple sources of information explored?

Which websites were searched?

Have specific (and relevant) websites been included in the report of the search for alternatives?

Was any other 'grey literature' included?

Has any 'grey literature' been mentioned? Did the search include pre-registered protocols, pre-prints of papers or information produced outside of traditional publishing and distribution channels, including reports, policy literature, newsletters, government documents, white papers or similar?

When were the articles published, and the search(es) completed?

What publication years were included?

Science and technology can progress rapidly, did the search involve the most up to date publications? What years of publication or release were included in the search?

When was the search conducted?

How long prior to the application being completed and submitted was the search conducted?

Was it repeated?

Was the search repeated at multiple time points, or was it carried out only once?

Who was approached for advice?

- Which networks, communities or individuals?**
Were any peers, or subject specific experts consulted? Or any of the expected beneficiaries of the research?
- Were any 3Rs or 1R organisations approached for expert advice?**
Several organisations exist to progress and promote the 3Rs, some of which focus solely on replacement. Where any of these organisations approached for advice?

How was the search conducted?

- What combination of operators and search terms was used?**
Were search terms combined appropriately?
- Were search string(s) constructed?**
Were the combined search terms and operators recorded?
- Were different types of searches used for different sources of information?**

Why were the results of the search(es) rejected?

- Were the results of the search provided?**
Have any references (papers, technical information) about potential techniques, or combinations of techniques, reported?
- Were the results relevant to the field?**
- Could any identified protocols be adapted to suit?**
What changes would need to be made to existing techniques in order to achieve research goals? Are any in development?
- If results were rejected, was it justifiable to do so? Was the output thoroughly evaluated?**
Has evidence of assessment been provided? Were any approaches found to be relevant to the research? What were the limitations of the approaches found? Would there be an opportunity to replace part of the overall programme of work?

It is important to remember that if a reported search for replacement techniques or alternative methods that avoid animal use falls short of being able to answer these questions, then it is worth asking what kind of support and training with respect to Replacement the researcher has received. If there is a gap in training, then researchers can be signposted to suitable courses or resources (e.g. EU-52: Searching for (existing) non-animal alternatives. Education and Training Platform in Laboratory Animal Science (ETPLAS), Cerdanyola del Valles, Spain. <https://learn.etplas.eu/courses/eu-52/>).